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### Neuroimaging: a potential new way for diagnosing bipolar disorder?

As current methods to diagnose bipolar disorder can lead to delays or misdiagnosis, new methods to diagnose it are a priority. In a recent study, researchers from the Icahn School of Medicine at Mount Sinai (NY, USA) reported that they were able to correctly distinguish bipolar patients from healthy controls using MRI.

The group applied Gaussian process classifiers to structural MRI data in two independent cohorts of patients (n = 26and 14, respectively) in order to evaluate the use of pattern recognition techniques for diagnosis. Within each cohort, patients were matched with an equal number of healthy controls for age, sex and IQ. The accuracy of the Gaussian process classifiers for gray matter was 73 and 72% in cohorts one and two, respectively, with a sensitivity and specificity, of 69 and 77% for cohort one, and 64 and 99% for cohort two, respectively. For white matter, the accuracy was 69% for cohort one (sensitivity: 69%; specificity: 69%) and 78% for cohort two (sensitivity: 71%; specificity: 86%).

Andy Simmons (Kings College London, London, UK), one of the study authors, noted that, "The level of accuracy we achieved is comparable to that of many other tests used in medicine." He also noted that, as brain scanning is a routine diagnostic test, it should be "very acceptable to patients." However, Sophia Frangou (Icahn Medical Institute), another member of the team, clarified that, "This approach does not undermine the importance of rigorous clinical assessment and building relationships with patients but provides biological justification for the

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type of diagnosis made." Frangou also

Frangou also confirmed the implications of the study: "diagnostic imaging for psychiatry is still under investigation and not ready for widespread use. Nonetheless, our results together with those from other laboratories are a harbinger of a major shift in the way we approach diagnosis in psychiatry." The group noted that future studies will be needed to replicate the findings in larger samples and

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across different sites. They will also be needed in order to evaluate the performance of pattern recognition classifiers for identifying subtypes of bipolar disorder and for differential diagnosis of bipolar disorder from overlapping clinical phenotypes. Source: Rocha-Rego V, Jogia J, Marquand AF, Mourao-Miranda J, Simmons A, Frangou S. Examination of the predictive value of structural magnetic resonance scans in bipolar disorder: a pattern classification approach. *Psychol. Med.* doi:10.1017/S0033291713001013 (2013) (Epub ahead of print).

# Recommendations reported for children with ADHD and traumatic brain injury

Researchers from the Children's Hospital of Pittsburgh (University of Pittsburgh, PA, USA) and the University of Chicago (IL, USA) have presented results stating that on suffering a mild traumatic brain injury (TBI), children with ADHD are more likely to demonstrate a moderate disability. The research could have implications for management of such patients.

Between January 2003 and December 2010, 48 children were identified as having ADHD alongside a diagnosis of mild closed-

head injury (CHI) at the Children's Hospital of Pittsburgh. These were paired with 45 randomly selected age-matched controls, who had mild TBI but no ADHD. The group recorded demographics, ini-

tial Glasgow Coma Scale score, hospital course and King's Outcome Scale for Childhood Head Injury score for a mean follow-up period of 24.9 weeks (7.2 weeks for those without ADHD).

Of the ADHD patients, 25% had a moderate disability and 56% were fully recovered, compared with 2 and 84% for the control group, respectively. The researchers explained that, "patients with ADHD were statistically significantly more disabled after mild TBI than were control patients without ADHD, even when controlling for age, sex, initial Glasgow Coma Scale score, hospital length of stay, length of follow-up, mechanism of injury and presence of other (extracranial) injury." The group postulated that ADHD might be associated with increased vulnerability to brain injury or impaired healing, or cause rehabilitation programs to be less effective.

The authors noted that, "This study highlights the importance of preventing TBI in children with ADHD, perhaps by encouraging them to avoid contact sports or hobbies that carry an increased risk of TBI. This is especially pertinent given the data showing that children with ADHD are reported to sustain higher levels of injury, especially CHI, when compared with age-matched controls. This study may better inform the clinical management in children who have ADHD and expe-

"...ADHD might be associated with increased vulnerability to brain injury or impaired healing, or cause rehabilitation programs to be less effective." rience a CHI, perhaps directing more intensive resources and closer monitoring to encourage maximal recovery. Third, it may spur the education of families of children with ADHD about

expectations during the recovery period after TBI. Finally, this study represents another reason to be aggressive about effective ADHD treatment; data exist showing that children with effectively treated ADHD have life outcomes comparable to children without ADHD." However, they also pointed out that, "Further studies are needed to evaluate the impact of ADHD and other conditions on outcome after TBI of increasing severity, and to explore the mechanisms underlying the relationship between these two conditions."

Source: Bonfield CM, Lam S, Lin Y, Greene S. The impact of attention deficit hyperactivity disorder on recovery from mild traumatic brain injury. *J. Neurosurg. Pediatr.* doi:10.3171/2013.5.PEDS12424 (2013) (Epub ahead of print).

# New discovery opens avenues for autism diagnostic tests

A study resulting from a collaboration between researchers from Greenwood Genetic Center (SC, USA) and Biolog, Inc. (CA, USA) has reported results that could lead to an early blood-screening test for autism spectrum disorders (ASDs). There is currently no laboratory test available for the diagnosis of ASDs, with diagnosis being dependent upon developmental evaluation and parental interview.

The group analyzed the metabolic profile of lymphoblastoid cell lines from 137 patients with neurodevelopmental disorders with (n = 87) or without ASDs and 78 normal individuals using Biolog Phenotype MicroArrays (Biolog, Inc.). The 87 ASD patients demonstrated reduced metabolism of L-tryptophan when compared with normal controls and cell lines from non-ASD patients with other

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neurodevelopmental disorders, such as intellectual disability and schizophrenia. An analysis of a subset of patients also demonstrated a lower expression of some genes involved in L-tryptophan metabolism.

Luigi Boccuto, lead author of the study, noted that, "The important and immediate implication of this work is the development of a simple, early blood-screening test for autism by measuring the metabolism of L-tryptophan using Biolog's technology." Early diagnosis would allow for provision of timely and effective therapy to patients.

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The discovery also has implications for potential future therapies. Boccuto

stated that, "Once we have a clear vision of what has gone awry within the tryptophan metabolism pathways, we can develop therapies to target and correct those problems at the biochemical level."

Source: Boccuto L, Chen CF, Pittman AR et al. Decreased tryptophan metabolism in patients with autism spectrum disorders. *Mol. Autism* 4(1), 16 (2013).

### Study examines the co-occurrence of ADHD and autism spectrum disorder

A group from the Kennedy Kreiger Institute (MD, USA) has reported interesting results that found that almost a third of children with autism spectrum disorder (ASD) have co-occuring symptoms of ADHD, and that children for whom both occur are significantly more impaired regarding measures of cognitive, social and adaptive function, compared with children who are ASD-only.

The researchers conducted a prospective, longitudinal study categorizing 162 children of 4–8 years of age into those with and without ASD; the 63 children with ASD were subsequently categorized by parent-reported ADHD classification. Eighteen patients had clinically significant symptoms of ADHD.

"We focused on young school-aged children because the earlier we can identify this subset of children, the earlier we can design specialized interventions," noted Rebecca Landa, corresponding author of the study. "Tailored interventions may improve their outcomes, which tend to be significantly worse than those of peers with autism only." The group also reported that those with co-occurrence of both ADHD and ASD were more impaired in cognitive and social functioning and the ability to function in everyday situations, and were more likely to have significant cognitive delays and display more severe autism mannerisms.

"Tailored interventions may improve [young children's] outcomes, which tend to be significantly worse than those of peers with autism only."

The authors suggest that children with a co-occurrence may require different treatment in order to receive the required outcomes, and that further research will be required in order to determine effective interventions to achieve this goal.

Source: Rao PA, Landa RJ. Association between severity of behavioral phenotype and comorbid attention deficit hyperactivity disorder symptoms in children with autism spectrum disorders. *Autism* doi: 10.1177/1362361312470494 (2013) (Epub ahead of print).

## Racing towards understanding biological causes of neurodevelopmental disorders

A recent symposium hosted by Roche (Basel, Switzerland) provided new insights into recent scientific advances in neurodevelopmental disorders, including autism spectrum disorders and Down's syndrome. The symposium brought together international experts from over 20 institutions as part of the Roche Autism Collaboration and Innovation Network, who are collaborating with Roche to shed light on biological causes of these disorders.

Luca Santarelli, Head of Roche Neuroscience and Small Molecule Research (F Hoffmann-La Roche Ltd., Basel, Switzerland), noted that Roche is committed to finding therapies for these neurodevelopmental disorders. "By collaborating with leading academic institutions and biotech companies, and forming public-private partnerships, we hope to improve our understanding of these

"...neurodevelopmental disorders are an area of high unmet medical need and Roche is committed to finding therapies for conditions such as autism spectrum disorder, Fragile X and Down's syndrome."

disorders enabling us to select the right targets and discover disease-modifying treatments that will benefit those suffering from these conditions."

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Research presented at the symposium included studies of autism spectrum disorder, using patient-derived induced pluripotent stem cells, which could lead to murine models that are useful for drug development, and could aid the intentions of the EU Autism Inventions consortium, which is geared toward developing new standards in clinical development, including a clinical trials network.

Currently, there are no effective pharmacological treatments that target the molecular basis of neurodevelopmental disorders.

As such, as Santarelli explains, "Neurodevelopmental disorders are an area of high unmet medical need and Roche is committed to finding therapies for conditions such as autism spectrum disorder, Fragile X and Down's syndrome."

Source: Roche Media Press Release. Roche demonstrates strong commitment to neurodevelopmental disorders. Roche, Basel, Switzerland (2013).

- All stories written by Francesca Lake

#### About the News

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